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## ORIGINAL ARTICLE

# Impact of herpes zoster and post-herpetic neuralgia on patients' quality of life: a patient-reported outcomes survey

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## Abstract

**Background** The impact of herpes zoster (HZ) and post-herpetic neuralgia (PHN) on patients' quality of life (QoL) is currently poorly documented.

**Subjects and methods** Telephone interviews in Germany identified patients  $\geq 50$  years old with painful HZ diagnosed during the previous 5 years. Bespoke questions evaluated previous HZ episodes.

**Results** Of 11,009 respondents, 280 met the screening criteria, and 32 (11%) developed PHN. PHN was associated with significantly worse outcomes than HZ (all  $P < 0.05$ ). Mean pain scores associated with PHN and HZ, respectively, were 7.1 and 6.2 (average) and 8.2 and 7.0 (worst). Many patients with PHN (91%) and HZ (73%) experienced problems with daily activities, including work, studies, housework, family and leisure activities. Mean pain interference scores in patients with PHN versus HZ were highest for

sleep (6.5 versus 4.9), normal work (6.1 versus 4.4) and mood (5.9 versus 4.4). Most employed interviewees with PHN (70%) and HZ (64%) stopped work during the disease. Pain and QoL outcomes were not significantly different between all patients versus those diagnosed during the previous 12 months or between patients aged 50–59 years versus  $\geq 60$  years.

**Conclusions** HZ causes substantial pain, which seriously interferes with many aspects of daily life, particularly in patients with PHN.

**Keywords** Herpes zoster · Pain · Post-herpetic neuralgia · Quality of life · Survey

## Background

Herpes zoster (HZ; 'shingles') is a reactivation of the latent varicella zoster virus (VZV; 'chicken pox') (Simpson 1954; Weller et al. 1958; Straus et al. 1984; Lungu et al. 1995). HZ is characterized by a vesicular skin rash, which is often preceded or accompanied by acute pain or itching. The most common and debilitating complication of HZ is post-herpetic neuralgia (PHN). There is no standard definition of PHN, but it is commonly defined as pain that persists for at least 3 months after the onset of HZ rash (Oxman et al. 2005; Gauthier et al. 2009). Patients with PHN report various pain types, including constant (burning, aching, throbbing), intermittent (e.g., stabbing, shooting) and pain induced by normally non-painful stimuli, such as cold wind or light touch from clothing (Schmader 2001; Dworkin et al. 2008).

In Western countries, the estimated incidence of acute HZ in the general population is 3–5 per 1,000 person-years (annual events per 1,000 population) (Gauthier et al. 2009; Hope-Simpson 1965; Paul and Thiel 1996; di Luzio Paparatti et al. 1999; Chidiac et al. 2001; Brisson and

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Edmunds 2003; de Melker et al. 2006; Yawn et al. 2007). HZ incidence increases with age because of a decline in specific immunity against latent VZV (Arvin 2005). There is a marked increase in annual risk starting at approximately 50 years of age that may reach >10 per 1,000 person-years in those aged  $\geq 80$  years (Gauthier et al. 2009; Hope-Simpson 1965; Paul and Thiel 1996; de Melker et al. 2006; Yawn et al. 2007). One in four people will contract HZ in their lifetime, with this risk rising to one in two individuals  $\geq 85$  years old (Schmader 2001; Miller et al. 1993). The risk of patients developing complications such as PHN increases with age (Gauthier et al. 2009; Choo et al. 1997). PHN incidence rises rapidly after the age of 60 years (Gauthier et al. 2009; Opstelten et al. 2002; Stein et al. 2009). Data show that 10–20% of patients with HZ aged  $\geq 50$  years will develop PHN that persists at 3 months (Oxman et al. 2005; Gauthier et al. 2009; Scott et al. 2006; Johnson and Rice 2007).

HZ and PHN can have a devastating effect on quality of life (QoL), affecting physical, functional, psychological and social domains (Schmader 2001; Oster et al. 2005; Coplan et al. 2004; Schmader 2002; van Seventer et al. 2006; Schmader et al. 2007; Lydick et al. 1995; Katz et al. 2004; Brisson et al. 2008). Patients have reduced functional ability, with many becoming inactive or housebound. QoL seems to be a particular problem in patients whose pain persists as PHN (Chidiac et al. 2001; Oster et al. 2005; Coplan et al. 2004; Schmader 2002; van Seventer et al. 2006; Mauskopf et al. 1994). Increased awareness of the burden of HZ and PHN on QoL may lead to improved strategies for prevention and management. The aim of this survey was to assess the impact of HZ and PHN on the QoL of a German population aged  $\geq 50$  years who had experienced painful HZ during the previous 5 years.

## Methods

### Interviews

Interviewers from TNS Healthcare Germany contacted randomly selected individuals in private German households between 25 March and 8 May 2008. In subjects who could answer questions by telephone, interviews lasted  $\leq 15$  min and comprised closed questions.

The applied standard system of TNS Healthcare Germany, ‘InfraScope’ (TNS Infratest 2004), combines computer-assisted telephone interviews with computer-assisted selection of addresses. It is based on the ‘Infratest-Telephon Master Sample,’ which was developed specifically for telephone surveys and leads to bias-free, representative samples. ‘Random-Digit Dialing’ reflects the standard Working Group of German Market and Social Studies

Institute, developed according to Gabler and Häder (Glemser 2002).

### Screening criteria

Patients eligible for the questionnaire had been diagnosed with HZ by a physician during the previous 5 years, had experienced HZ-related pain and were  $\geq 50$  years old. Initially, only patients with HZ diagnosed during the previous 12 months were included, but this criterion was changed to obtain the required sample size in a shorter timeframe ( $n = 280$ ). Eligible respondents were classified as patients with HZ (if pain lasted <3 months after rash onset) or patients with PHN (if pain lasted  $\geq 3$  months after rash onset).

### Questionnaire

Bespoke questions were developed. Some questions were informed from standard QoL questionnaires and developed further to enable evaluation of previous HZ episodes.

Patients were asked questions to assess the characteristics of HZ/PHN pain. Patients also rated pain level on a scale from 0 (‘no pain’) to 10 (‘pain as bad as you can imagine’). Receipt of treatments or medications and the pain relief that they provided were also assessed.

Further questions assessed the impact of HZ and PHN on QoL. These included problems with usual daily activities (work, studies, housework, family and leisure activities), mobility and self-care, and the degree of pain/discomfort and anxiety/depression. Limitations in the activities of daily living were also assessed (including moderate physical efforts and climbing flights of stairs) and consequences for family members and the social circle of the patient. Patients rated interference of pain from 0 (‘does not interfere’) to 10 (‘completely interferes’) in the following seven areas: general activity, mood, walking ability, normal work, social relations, sleep and enjoyment of life. Patients were asked about the impact of HZ and PHN on work and sleep, as well as feelings of stress and enjoyment. Patients rated the impact of HZ and PHN on their overall QoL from 0 (‘not affected at all’) to 10 (‘highly affected’).

QoL data are presented for the following categories: daily activities, mobility, work, sleep, mood, social/family relations and overall QoL.

### Statistical analysis

To identify 280 patients eligible for the main questionnaire (approximately 50% aged 50–59 years and 50% aged  $\geq 60$  years), 11,009 subjects aged  $\geq 50$  years were contacted and screened. Proportions and means were tested on a 90% confidence level to assess if there were significant differ-

ences in pain and QoL outcomes between the following subgroups: (1) all patients versus only the proportion with HZ diagnosed during the previous 12 months; (2) patients 50–59 years of age versus those  $\geq 60$  years of age; (3) patients with HZ versus those whose pain persisted as PHN.

Multiple regression analysis was carried out on the outcome of pain interference to assess which aspects had a significant impact on QoL rating. Measurement was by standardized  $\beta$ -coefficients. Normalized values (e.g., areas that have an impact on overall QoL) were set as 100%.

## Results

### Patient characteristics

A total of 11,009 respondents  $\geq 50$  years of age were interviewed to identify 288 (2.6%) patients who had experienced painful HZ diagnosed by a physician during the previous 5 years. Pain duration after rash onset was  $< 3$  months in 248 (89%) respondents (patients with HZ),  $\geq 3$  months in 32 (11%) respondents (patients with PHN) and unknown in 8 (3%) respondents. Eight patients could not be classified as having HZ or PHN, so results are presented for 280 patients. Of these, 102 (36%) patients were diagnosed with HZ during the previous 12 months. Approximately equal numbers of patients were aged 50–59 years ( $n=130$ ; 46%) and  $\geq 60$  years ( $n=150$ ; 54%).

Patient characteristics are displayed in Table 1. Most patients were women (HZ, 64%; PHN, 81%), and mean age was 63.5 years. There were no relevant differences in characteristics between patient subgroups. Most patients aged 50–59 years were employed full time (62%) and some part time (11%), whereas most of those  $\geq 60$  years of age were retired (81%).

### Subgroup analysis of pain and QoL outcomes

Patients' recollection of HZ pain and the impact of disease on QoL were not affected by time since diagnosis or by age. Outcomes were therefore similar for all patients versus those diagnosed only within the previous 12 months and for patients aged 50–59 years versus those aged  $\geq 60$  years. In contrast, patients with PHN had statistically significantly worse outcomes on every pain and QoL measure than patients with HZ.

### Patient-reported pain and treatment

In 60% of patients, HZ pain was spontaneous, with some patients reporting spontaneous pain that increased with friction (30%), pressing (28%) or contact with a cold object

(6%). HZ pain was described as 'burning' by 58% of patients, as 'electric shocks' by 13% and as 'painful cold' by 8% of patients.

Pain levels were considerable, with mean pain scores in all patients, patients with HZ and those with PHN, respectively, of 6.3, 6.2 and 7.1 on average, and 7.2, 7.0 and 8.2 at worst ( $P < 0.05$  for patients with HZ versus PHN). High levels of pain (score 8–10) on average and at worst were reported by greater proportions of patients with PHN than with HZ (Table 2A).

Although 97% of patients received treatment for HZ, 41% did not receive treatment within 3 days of rash onset. Approximately 45% of patients required more than one medication. Patients with PHN received significantly more medications than patients with HZ (mean: 2.2 versus 1.6, respectively,  $P < 0.05$ ) and yet experienced significantly less pain relief (49% versus 67%,  $P < 0.05$ ).

### Impact of HZ and PHN on QoL

#### *Interference with daily activities*

Patients with PHN experienced a significantly higher level of pain interference with general activity than those with HZ ( $P < 0.05$ ) (Fig. 1). Multiple regression analysis showed that, of the seven areas assessed, general activity had the highest significant impact on QoL rating (33%; adjusted  $R^2$  0.57).

High proportions of patients experienced problems in their usual daily activities (75%) and self-care (56%). Patients with PHN had a greater prevalence of these problems than those with HZ: usual daily activities (91% versus 73%) and self-care (75% versus 54%). Many patients were limited in moderate physical efforts (68%) such as climbing flights of stairs (43%) (Table 2B).

#### *Mobility*

Patients with PHN experienced significantly greater pain interference with walking ability than those with HZ ( $P < 0.05$ ) (Fig. 1). The impact of walking ability on QoL rating was not significant according to multiple regression analysis. High proportions of patients experienced problems with mobility (63% overall), particularly those with PHN (78% versus 61% of those with HZ). In 19% of patients with PHN, mobility was sufficiently severe that they were confined to bed.

#### *Work*

Of the 39% of interviewees who were employed while affected by HZ/PHN, 65% reported absence from work because of their disease. This was mainly due to pain (60%), discomfort (60%), inability to concentrate (48%)

**Table 1** Patient characteristics

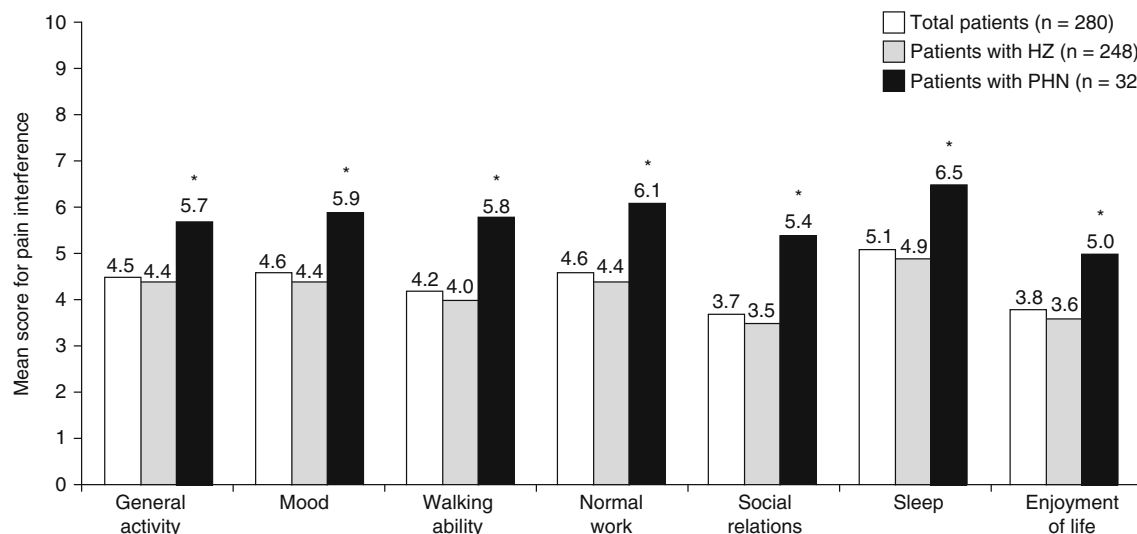
	All	HZ within previous 12months	Age (years) 50–59	≥60	Patient category	
					With HZ	With PHN
All patients, n (%)	280 (100)	102 (36)	130 (46)	150 (54)	248 (89)	32 (11)
General characteristics						
Sex, n (%)						
Female	185 (66)	69 (68)	81 (62)	104 (69)	159 (64)	26 (81)
Male	95 (34)	33 (32)	49 (38)	46 (31)	89 (36)	6 (19)
Age, years, mean (SD)	63.5 (9.6)	63.5 (9.8)	54.9 (2.8)	70.9 (6.9)	63.5 (9.6)	63.3 (10.0)
Working status, %						
Employed full-time (≥30 h per week)	33	35	62 <sup>a</sup>	7	34	22
Employed part time (<30 h per week)	6 <sup>a</sup>	3	11 <sup>a</sup>	2	5	13
Not working/housewife/house husband	4	3	2	5	3	6
Unemployed	4	4	8 <sup>a</sup>	1	4	3
Retired	51	53	15	81 <sup>a</sup>	50	53
Not employed, reason not known	2	1	2	2	2	-
Other	0	1	1	-	-	3 <sup>a</sup>

<sup>a</sup> Significant differences between subgroups (all patients versus only the proportion with HZ diagnosed during the previous 12 months; patients aged 50–59 years versus those aged ≥60 years; and patients with HZ versus those whose pain persisted as PHN)

**Table 2** Pain and QoL outcomes

	All ( <i>n</i> =280)	HZ within previous 12months ( <i>n</i> =102)	Age (years) 50–59 ( <i>n</i> =130)	≥60 ( <i>n</i> =150)	Patient category	
					With HZ ( <i>n</i> =248)	With PHN ( <i>n</i> =32)
A. Level of pain						
Pain score (0–10 scale), mean						
On average	6.3	6.6	6.3	6.3	6.2	7.1*
At worst	7.2	7.3	7.3	7.0	7.0	8.2*
High pain level (score 8–10), % patients						
On average	31	36	29	31	29	41
At worst	49	52	52	49	48	62
B. Limitations experienced on activities of daily living						
Moderate physical efforts, <sup>a</sup> % patients						
Limited at least a bit <sup>b</sup>	68	66	67	68	65	85
Limited a lot	25	28	23	27	23	41*
Climbing flights of stairs, % patients						
Limited at least a bit <sup>b</sup>	43	45	45	41	40	65
Limited a lot	14	14	15	14	12	31*
Consequences for family members and social circle, % patients	53	53	53	54	50	81
C. Feelings of stress and enjoyment of leisure activities						
Stressed at some time <sup>c</sup> , % patients	80	81	80	79	78	91
Stressed most of the time, % patients	22	21	20	23	19	41*
Did not enjoy leisure activities <sup>d</sup> , % patients	37	31	42	33	36	47

\* $P < 0.05$  versus corresponding group. <sup>a</sup> Moderate physical efforts include repositioning a table, vacuum cleaning and playing bowling. <sup>b</sup> Physical efforts limited at least a bit includes 'a bit' and 'a lot.' <sup>c</sup> Stressed at some time includes 'most of the time,' 'long time' and 'sometimes.' <sup>d</sup> Did not enjoy leisure activities includes 'rarely enjoyed' and 'very rarely enjoyed;' leisure activities include reading a book, listening to the radio or watching TV



**Fig. 1** Effect of HZ/PHN pain on seven aspects of QoL (0–10 scale). \* $P < 0.05$  for patients with PHN versus HZ

and health care visits (48%). Patients with PHN experienced a significantly higher level of pain interference with normal work than those with HZ ( $P < 0.05$ ) (Fig. 1). The impact of normal work on QoL rating was not significant according to multiple regression analysis.

#### Sleep

For many patients, sleep was ‘not quiet’ for at least some of the time (overall, 60%; HZ, 57%; PHN, 88%) and for most of the time (overall, 25%; HZ, 22%; PHN, 53%). Overall, 65% of patients did not have sufficient sleep most of the time (HZ, 63%; PHN, 78%). Patients with PHN experienced a significantly higher level of pain interference with sleep than patients with HZ ( $P < 0.05$ ) (Fig. 1). A significant impact of sleep on QoL rating was shown by multiple regression analysis (18%; adjusted  $R^2$  0.57).

#### Mood

Patients with PHN experienced significantly higher levels of pain interference with mood and enjoyment of life than those with HZ (both  $P < 0.05$ ) (Fig. 1). Multiple regression analysis showed a significant impact of mood (20%) and enjoyment of life (16%) on QoL rating (adjusted  $R^2$  0.57).

Anxiety or depression as a result of HZ/PHN was experienced by 40% of all patients; the proportion of patients affected was higher for PHN than HZ (57% versus 37%). Eighty percent of patients experienced stress during the time they had HZ pain, particularly those with PHN (91% versus 78% of those with HZ) (Table 2C). Overall, 37% of patients could not enjoy simple activities such as reading a book, listening to the radio or watching television, while suffering from HZ/PHN.

#### Social/family relations

Patients with PHN experienced significantly higher levels of pain interference with social relations than patients with HZ ( $P < 0.05$ ) (Fig. 1). A significant impact of social relations on QoL rating was shown by multiple regression analysis (13%; adjusted  $R^2$  0.57). Fifty-three percent of patients reported that HZ/PHN had consequences for family members and their social circle; the proportion of patients affected was greater for PHN than for HZ (81% versus 50%,  $P < 0.05$ ) (Table 2B).

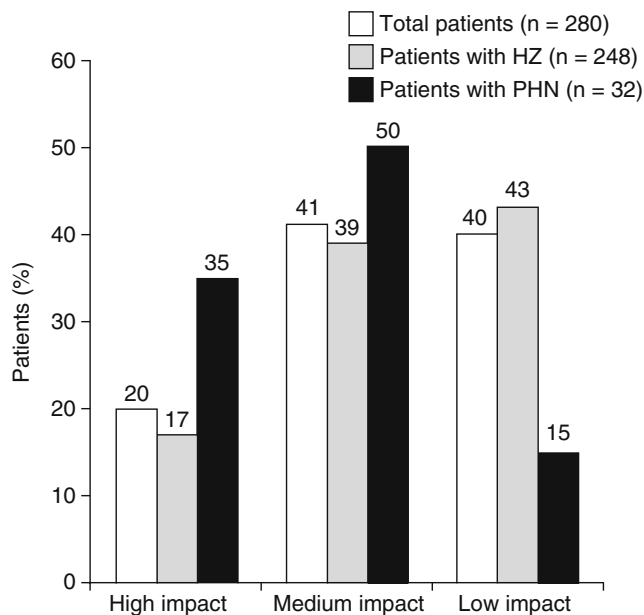
#### Overall impact of QoL

The impact of HZ/PHN on patients’ overall QoL was considerable, with a mean affection score of 4.5 in all patients and 4.2 versus 6.1 in patients with HZ versus PHN, respectively ( $P < 0.05$ ). Greater proportions of patients with PHN than HZ reported that their QoL was affected to a high level (35% versus 17%) or medium level (50% versus 39%) (Fig. 2).

#### Discussion

This scientific survey assessed the impact of HZ and PHN on the QoL and daily life of a German population aged  $\geq 50$  years who had experienced painful HZ during the previous 5 years. This retrospective approach enabled information to be captured on the full course of HZ episodes, from rash onset to pain resolution. Patient-reported outcomes clearly showed that HZ causes substantial pain that seriously interferes with many aspects of patients’ daily life, particularly sleep, mood and work. Pain and QoL outcomes were not affected by time since diagnosis or by age. Patients with PHN had considerably





**Fig. 2** Proportion of patients whose HZ had a high (score 8–10), medium (score 4–7) and low (score 0–3) impact on overall QoL

worse outcomes on every measure of pain and QoL than those with HZ.

Studies suggest that high levels of patient-reported pain and QoL burden are associated with HZ (Schmader 2001; Chidiac et al. 2001; Coplan et al. 2004; Schmader et al. 2007; Lydick et al. 1995; Katz et al. 2004) and PHN (Chidiac et al. 2001; Oster et al. 2005; Coplan et al. 2004; van Seventer et al. 2006; Mauskopf et al. 1994). In one study, acute HZ pain affected all domains of patients' activities of daily living (Lydick et al. 1995). There was a clear correlation between increased intensity of pain and greater interference with activities. The devastating effects of HZ pain on patients' QoL were comparable to the effects of myocardial infarction and clinical depression. Two observational studies that employed various QoL questionnaires demonstrated a substantial pain burden of HZ in the first 30 days after rash onset, with moderate and severe levels of pain commonly experienced (Schmader et al. 2007; Katz et al. 2004). In a study by Schmader et al. (2007), worst pain 7 days after rash onset in 102 patients with HZ (0–10 pain scale) was moderate (score 4–7) in 48 patients and severe (score 8–10) in 19 patients. Pain interfered with all activities of daily living, particularly enjoyment of life, sleep, general activities, leisure activities, leaving the house and going shopping. In a study by Katz et al. (2004), patients experienced average pain of moderate intensity most of the time. Regression analysis showed that significant independent contributions were made by sensory pain burden to poorer physical functioning, overall pain burden to poorer role and social functioning, and affective pain burden to depression.

Greater levels of acute pain may contribute to the development and severity of PHN. Psychosocial variables such as measures of role functioning, personality disorder symptoms and disease conviction may be additional risk factors for PHN (Katz et al. 2005). This chronic complication remains refractory to pharmacological treatments and prevention strategies (Johnson and McElhaney 2009). PHN is thought to be associated with numerous constitutional symptoms (chronic fatigue, anorexia, weight loss, physical inactivity, insomnia) and psychological symptoms (depression, difficulty concentrating). PHN may interfere with basic activities (e.g., dressing, bathing, mobility) and more complex activities (e.g., traveling, shopping, cooking, housework, social functioning) (Schmader 2002). Results from a postal survey in the USA that used pain and QoL questionnaires showed that patients commonly reported moderate and severe levels of pain despite receiving analgesic agents (Oster et al. 2005). PHN burden was substantial and multidimensional, with all domains of daily functioning and health status negatively affected. There was a positive correlation between increasing pain severity and the extent of the negative QoL impact. An observational study that used patient questionnaires showed that the mean pain level in patients with PHN was moderate (score 4.2) (van Seventer et al. 2006). Seventy-eight percent of patients reported the worst pain as moderate to severe. Pain interference was reported on all seven domains of health status, particularly mood, sleep and general activity. The overall EuroQoL health valuation was 0.60. Substantial proportions of patients received medications for depression, anxiety and sleep disturbances related to PHN.

The burden of HZ and PHN is particularly important given that HZ will manifest in one in four people within their lifetime (Schmader 2001; Miller et al. 1993) and that 10–20% of patients with HZ  $\geq 50$  years old will experience PHN (Oxman et al. 2005; Gauthier et al. 2009; Scott et al. 2006; Johnson and Rice 2007). The prevalence of HZ and PHN is expected to increase with the rising mean age of the population (Brisson et al. 2001).

This retrospective survey has shown that pain levels in patients with HZ were unacceptably high, particularly in those who developed PHN. HZ treatment using antiviral agents may reduce acute pain if given within 72 h of rash onset (Christo et al. 2007; Breuer and Whitley 2007), but probably will not ameliorate subsequent PHN (Johnson and McElhaney 2009). Many patients in the present survey did not receive treatment within this time window, nearly half of patients needed more than one pain medication and patients with PHN experienced significantly less pain relief than patients with HZ, despite receiving more medications. Furthermore, the direct impact of existing HZ treatments on QoL is not well studied.

Questions inspired by standard questionnaires consistently showed that HZ and PHN had a substantial impact on daily

activities, mobility, work, sleep, mood, social/family relations and overall QoL. Mean pain interference was highest for sleep, mood and normal work. Multiple regression analysis revealed that general activity, sleep, mood, enjoyment of life and relations with others all had a significant impact on QoL rating. Patients with PHN had considerably worse outcomes on every QoL measure compared with patients with HZ. Pain and QoL data from patients diagnosed in the previous 12 months were consistent with data from all patients. This demonstrated that patients' recollection of the impact of disease was not affected by time.

The high burden of HZ and PHN demonstrated in the present study is similar to the findings from the observational studies discussed above (van Seventer et al. 2006; Schmader et al. 2007; Katz et al. 2004). The present survey proved to be a useful tool for assessing patient-reported outcomes in HZ and PHN. Therefore, the questionnaire has been translated and adapted for use in six other countries. In lieu of prospective studies, retrospective studies can provide information more rapidly and with a larger sample size, and may give important leads for the design of a prospective study on the impact of HZ and PHN on patients' QoL.

This study had certain limitations. First, there was a relatively high proportion of patients diagnosed with HZ in the previous 12 months versus the total number of patients diagnosed in the last 5 years. This was because the screening criterion regarding length of time since diagnosis was changed after initial interviews to obtain the required sample size in a shorter timeframe. Second, we evaluated the full course of HZ episodes, and thus were not able to use currently available validated questionnaires to evaluate pain and QoL, which only evaluate current pain. However, this approach allowed a better view of the patient's global experience of their illness and follows the approach taken in the pivotal SPS study that assessed the HZ burden of illness using a severity-by-duration measure (Oxman et al. 2008). Third, patients were required to recall information about their HZ disease from up to 5 years before the interviews. However, data clearly showed that patients' recollection of pain associated with HZ and PHN and the impact of disease on QoL were not affected by time. Finally, two-thirds of patients with HZ were female. Studies have shown a higher prevalence of HZ in women than in men (Gauthier et al. 2009; Bowsher 1999). In the present telephone survey, many more women than men aged  $\geq 50$  years may have been willing to discuss their health.

## Conclusions

Patients with HZ have high levels of pain, and this affects many areas of their lives, including daily activities, mobility, work, sleep and mood. Results of this survey clearly showed that the development of PHN is consistently associated with

worse outcomes than HZ. This survey will contribute to an increased awareness of the significant burden that patients with HZ and PHN suffer. Recognition of this burden may lead to improved prevention and management strategies.

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**Conflict of interest information** T. Weinke has received honoraria or consulting fees from GlaxoSmithKline, Novartis Vaccines and Sanofi Pasteur MSD. A. Edte is an employee of TNS Healthcare who conducted this study. S. Schmitt and K. Lukas are employees of Sanofi Pasteur MSD, a provider of a herpes zoster vaccine approved in the European Union.

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